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POSTER PRESENTATION

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# The blood of healthy individuals exhibits CD8 T cells with a highly altered TCR V $\beta$ repertoire but with an unmodified phenotype

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CD8 T cell clonal expansions (TCE) have been observed in elderly, healthy individuals as well in old mice, and have been associated with the ageing process. Both chronic latent and non-persistent viral infections have been proposed to drive the development of distinct non-functional and functional TCE respectively. Biases in TCR V $\beta$  repertoire diversity are also recurrently observed in patients that have undergone strong immune challenge, and are preferentially observed in the CD8 compartment. Healthy adults can also exhibit CD8 T cells with strong alterations of their CDR3 length distribution. Surprisingly, no specific investigations have been conducted to analyze the CD8 T cell repertoire in normal adults, to determine if such alterations in TCR V $\beta$  repertoire share the features of TCE. In this study, we characterized the phenotype and function of the CD8 population in healthy individuals of 25-52 years of age. All but one of the EBV-positive HLA-B8 healthy volunteers that were studied were CMV-negative. Using a specific unsupervised statistical method, we identified V $\beta$  families with altered CDR3 length distribution and increased TCR V $\beta$ /HPRT transcript ratios in all individuals tested. The increase in TCR V $\beta$ /HPRT transcript ratio was more frequently associated with an increase in the percentage of the corresponding V $\beta$ <sup>+</sup> T cells than with an absence of modification of their percentage. However, in contrast with the previously described TCE, these CD8<sup>+</sup> T cells were not preferentially found in the memory CD8 subset, they exhibited normal effector functions (cytokine secretion and cytotoxic molecule expression) and they were not reactive to a pool of EBV/CMV/Flu virus peptides. Taken together, the

combined analysis of transcripts and proteins of the TCR V $\beta$  repertoire led to the identification of different types of CD8<sup>+</sup> T cell clone expansion or contraction in healthy individuals, a situation that appears more complex than previously described in aged individuals.

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